improved diagnostic accuracy provided by the dual combination of tumour diameter and imaging characteristics, which is currently the most widely used approach in clinical practice, with an unenhanced CT tumour attenuation threshold of 20 Hounsfield units (HU) instead of the recommended 10 HU, is the more directly relevant and clinically practical finding from the study. Indeed, there remains a long way to go before assessment of urine steroid metabolomics with mass spectrometry could be routinely implemented in clinical practice. In addition to the limitations discussed in the accompanying commentary,[2] we are concerned about the cost-effectiveness of such an approach, which will require more affordable mass spectrometry to be available in clinical laboratories. Furthermore, the incorporation of steroid metabolomics into clinical practice will require validation of assay reproducibility and the subsequent introduction of population-based, age-specific, and sex-specific reference values for the adult steroid metabolome.[3]

Additionally, we note that patients with current or recent (<6 months) intake of drugs known to alter steroid synthesis or metabolism were excluded from the study. Could the investigators specify which drug categories were included in this exclusion criterion? Treatment with systemic glucocorticoids or drugs known to alter steroid secretion, such as hormonal menopause treatment, antiepileptic drugs, ketoconazole, and mineralocorticoid receptor antagonists (spironolactone or eplerenone) might compromise the diagnostic performance of urine metabolomics.[3,4] However, use of these drugs is not uncommon among individuals of a similar age to those included in the study (median age 59 years). Finally, we would be grateful if the investigators could provide information on participants' renal function, since advanced chronic kidney disease might affect steroid metabolite secretion in the urine.

We declare no competing interests.

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Authors' reply

We are grateful to Panagiota Anyfanti and colleagues for their interest in our work[1] and their useful comments. We agree that our findings with respect to the unenhanced CT tumour attenuation threshold should have a major impact on clinical practice. These results, based on data from more than 2000 prospectively recruited participants, justify an immediate change in practice, with maximum tumour diameter of 4 cm and unenhanced CT tumour attenuation of 20 Hounsfield units (HU) as the most appropriate threshold values for consideration of adrenocortical carcinoma as a differential diagnosis in patients with newly diagnosed adrenal masses. We showed that, compared with the currently recommended cutoff of 10 HU, a tumour attenuation value greater than 20 HU on unenhanced CT had considerably higher specificity (80·0% [95% CI 77·9–82·0%] *vs* 64·0% [61·4–66·4]) while maintaining similar sensitivity (99·0% [94·4–100·0] *vs* 100·0% [96·3–100·0]). Introducing a more specific cutoff into clinical practice should result in a decrease in the number of imaging procedures and surgeries in patients eventually diagnosed with benign adrenal masses. In view of our findings, work on the timely revision of the international guidelines on the management of adrenal incidentalomas[2] is underway.

Our study[1] also provides a definitive prospective validation of urine steroid metabolomics—the combination of mass spectrometry-based multisteroid profiling with steroid data analysis by a machine learning-based algorithm. We showed that urine steroid metabolomics had twice the positive predictive value of either tumour diameter or imaging characteristics including unenhanced tumour attenuation in the detection of adrenocortical carcinoma and that the combination of these three tests provided the highest diagnostic accuracy, which should be reflected in future international guideline recommendations.

Impaired kidney function was not an explicit exclusion criterion for enrolment in the EURINE-ACT study. However, we do not anticipate that chronic kidney disease will compromise the diagnostic accuracy of our approach, except in patients on kidney replacement therapy. Steroid profiling in patients with chronic kidney disease previously showed minor changes affecting glucocorticoid metabolism,[3] which are unlikely to affect test results. Diagnostic assessment by urine steroid metabolomics is based on the detection of changes in the pattern of steroid excretion, specifically the propensity of adrenocortical carcinomas to overproduce a distinct set of precursor steroids, rather than absolute quantitative cutoffs for individual steroid metabolites that might or might not be affected by impaired renal function.

We excluded any patients taking drugs that could affect steroid biosynthesis and metabolism. In clinical practice, intake of glucocorticoids and inhibitors of key branch points of steroidogenesis, such as ketoconazole and metyrapone, could affect the accuracy of our approach. However,

we have previously shown[4] that mitotane treatment does not affect the malignant steroid fingerprint and recently provided proof of principle for the use of urine steroid metabolomics for recurrence detection in patients with completely resected adrenocortical carcinoma.[5]

The machine learning-based algorithm we used for the diagnostic interpretation of urine steroid profiling results was developed from data from a retrospectively collected cohort of patients with adrenocortical adenomas and carcinomas,[6] prior to its prospective validation in the EURINE-ACT study.[1] Age-based and sex-based reference ranges are irrelevant to the diagnostic use of our algorithm. In our previous proof-of-principle study[6] on the use of urine steroid metabolomics for the differentiation of benign and malignant adrenocortical tumours, we showed that the malignant steroid fingerprint detected in patients with adrenocortical carcinoma is orders of magnitude higher than the relatively minor differences in steroid metabolite excretion seen between sexes and adult age groups.

We acknowledge that global rollout of urine steroid metabolomics will depend on the regional availability of mass spectrometry technology, but we are confident that its rollout across Europe can be achieved fairly soon, primarily implemented through a network of expert laboratories delivering centralised service provision and maintaining quality control through cross-validation and certification.

For the **beSafeMoris** app see https://besafemoris.mu/

Published **Online** September 24, 2020 https://doi.org/10.1016/S2213-8587(20)30336-3

WA is an inventor and MB is a contributor on a patent on the use of steroid profiling as a biomarker tool for the differential diagnosis of adrenal tumours (PCT/GB2010/000274). All other authors declare no competing interests. The views expressed are those of the authors and not necessarily those of the study funders.

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Tackling the COVID-19 pandemic in paradise: the Mauritian experience

Mauritius is a subtropical island located in the southwestern Indian Ocean, with a multiethnic population of about 1·3 million people. Mauritius also has one of the highest prevalences of diabetes worldwide,[1] a condition linked to the severity of COVID-19.[2]

Despite the challenges in curbing the COVID-19 pandemic, Mauritius scored a very high mark on the Oxford COVID-19 Government Response Stringency Index[3] in the middle of April, 2020. In part, this success was due to a prompt and consistent governmental strategy.

On Jan 21, all passengers arriving from China were quarantined for 14 days under strict sanitary conditions. 1 day later, the Prime Minister of Mauritius chaired a high-level committee meeting with all his ministers, as well as a representative from WHO to discuss approaches to control the pandemic. Because Mauritius is a very popular tourist destination, it was vital to control the arrival of overseas travellers with COVID infection. Temperature checks for passengers arriving at the international airport were introduced, and all visitors from high risk countries (eg, Singapore, Malaysia, and Thailand) were also quarantined from Feb 11.

On March 18, the first three cases of COVID-19 were registered in travellers and consequently on March 19, the borders were closed. With the escalation of cases, a curfew was imposed on March 20, and eventually a complete lockdown was implemented on March 24.

Mauritius and its citizens also stood firm against the pandemic. Work access permits were essential to avoid heavy fines and legal action. Health services were fully functional including a hotline telephone service to answer public queries. Between March 21, and July 20, 99 678 calls were received and attended to. A home visit team was set up which provided domiciliary visits consultations, and basic treatment. A mobile application, beSafeMoris was launched on March 26, allowing the Mauritian population to obtain real-time information about health and safety measures.

In parallel, regional public health superintendents and several rapid response teams were responsible for the transfer of patients with suspected COVID-19 to quarantine and treatment centres and a contact tracing team aimed to identify related cases. WHO infection control standard precautions were strictly followed during the pandemic.[4]